# When to test women for human papillomavirus

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# When to test women for human papillomavirus

*Cervical screening using HPV testing shows great promise but warrants caution*

*Research* pp 79, 83

Increased understanding of human papillomaviruses (HPV) and cervical carcinogenesis has led to prevention strategies that are very promising. Two articles in this issue (pp 79, 83) find that DNA testing for HPV is a cost effective way to clarify the meaning of equivocal results of cervical cytology.[1 2]

Cervical HPV infections are very common, particularly among young women, and are sexually transmitted.[3] They usually clear within one or two years. However, persistent infections by 15 or so carcinogenic HPV genotypes cause most cases of cervical precancer, which is generally diagnosed years after the causal infection, and of invasive cancer, which is typically diagnosed at least two decades after infection.[4]

Reproducible methods for testing for HPV are already available that are more sensitive (but less specific) than cytology for detecting prevalent and incipient precancer and cancer.[5] Testing for HPV might be used to improve the four sequential steps of programmes for preventing cervical cancer: population screening, triaging equivocally abnormal cytology, diagnosing women with abnormal results linked to deciding when to treat, and assuring cure after treatment. Until recently, the standard model for prevention was based on identifying morphological changes in cervical cells. This model comprises cytology for screening, repeated cytology to triage equivocal results, colposcopy and biopsy for histological diagnosis and treatment decisions, and cytology or colposcopy to assess cure. Other strategies based on HPV testing are gaining empirical support.

Cytology (Pap smear) screening has greatly reduced rates of cervical cancer in regions with well organised, population-wide programmes. Because cytology is limited by moderate sensitivity and poor reproducibility, the effectiveness of such programmes relies on many rounds of screening throughout adulthood. Testing for HPV is a more sensitive and reproducible tool than cytology for cervical precancer and cancer and is theoretically a better primary screening test if applied with proper understanding of the clinical course of HPV infection.

For example, HPV screening should not begin until 10-15 years after the average age of sexual debut, past the ages of frequent acquisition and clearance of HPV infection. Efficiency of HPV testing increases with age because the prevalence of benign, recently acquired infections declines as the prevalence of precancer and treatable cancers rises. These trends together increase the predictive value of a positive HPV test but maintain the reassurance provided by a negative test, which in turn permits the lengthening of screening intervals.[6]

If HPV testing is used for primary screening the management of women found to be positive for carcinogenic types of the virus will depend on regional resources. To increase the specificity of screening for HPV, positive women can be triaged by using Pap tests[7]; if they are cytologically negative, they can be rescreened by HPV testing a year or two later to identify persistent infection. When assays for specific types of HPV become available, persistent infection with the most carcinogenic types, such as HPV16 and HPV18, would imply a particularly high risk of cancer. Where diagnostic resources are limited, women aged 35 and above might have HPV testing in the context of screen and treat strategies because, in many populations, a positive HPV test at older ages will probably represent persistent infection and an associated raised risk of precancer or treatable cancer.[8]

When the results of screening cytology are equivocal, "reflex" HPV testing is cost effective in deciding whether colposcopy is needed, as confirmed by the two articles in this issue.[1 2] True precursors of cervical cancer (and the cancer) are caused by carcinogenic HPV; "look alike" cells are negative for carcinogenic HPV. In any setting HPV testing is useful only to clarify results for the cytological categories that harbour true uncertainty. Technical efficacy of triage is no longer questionable, but the cost effectiveness of triage by HPV testing compared with cytological or colposcopic methods will vary between populations and regions.

Recent improvements in screening for cervical cancer have not been matched by concomitant advances in colposcopic evaluation and diagnosis. Indeed, the sensitivity of biopsy directed by colposcopy to detect underlying precancer is only around 70%.[9] Thus, despite its historical status as the diagnostic gold standard, this procedure is now a technically weak link in the prevention of cervical cancer. Cost effectiveness analyses should be adjusted to reflect these limitations.

If the reproducibility and sensitivity of HPV testing proves to be superior to the combination of cytology and colposcopy, are we willing to treat women surgically—and remove the entire zone of cancer susceptibility, the cervical squamocolumnar transformation zone—on the basis of virological risk status alone? In general, the specificity and positive predictive value of HPV testing are mediocre. But there are notable exceptions: for example, even in the absence of

*BMJ* 2006;332:61–2

histologically confirmed precancer, women with abnormal cytology and HPV16 infection are at very high absolute risk of having a missed, small precancerous lesion (cervical intraepithelial neoplasia grade 3).[10]

After excisional or ablative treatments of the cervix for precancer, the absolute risk of recurrence is about 5-10%. Testing for HPV four to six months after treatment is highly sensitive and specific for the risk of recurrence and is better than cytology alone for monitoring cure.[11]

Regardless of their promise, switching to prevention strategies based on HPV testing warrants caution. Only one test has had extensive clinical validation. Before widespread adoption, all new HPV tests will require robust, real life evidence of reliability and accuracy in detecting precancer and cancer; otherwise, testing errors could mislead clinical management.[12] Furthermore, even the low cost HPV tests now being developed will have to be used in targeted populations if they are to be cost effective. Excessive or misguided use will increase costs without adding benefit. Like most revolutionary technologies, HPV testing must be managed wisely to do good rather than harm.

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# Primary care for refugees and asylum seekers

*If the NHS stops free care for all groups, charities may offer the only safety net*

*Analysis and comment* p 115

The decision by Médecins du Monde to open medical clinics in Tower Hamlets, east London, as an alternative to NHS primary care raises profound questions about society's attitude towards marginalised people.[1] Médecins du Monde is best known for relief work in areas of disaster or war and in developing countries. Less well known are this non-governmental organisation's projects in European countries—more than 100 in France alone—for groups with restricted access to health care. Alongside its humanitarian clinical work, the organisation is committed to speaking out about social and political conditions in which its client populations live, and calling for changes to improve their circumstances.[2]

Inequality in access to health services is not a new problem for east London, where inadequate recruitment and retention in general practice make access to the NHS difficult for the whole population.[3] Médecins du Monde will focus on vulnerable migrants, including asylum seekers and refugees, and particularly on failed asylum seekers and other people staying longer than allowed. The difficulties faced by these groups in gaining access to primary care have been well documented.[4] In much of Tower Hamlets, general practices are at full capacity or may be able to provide only temporary registration with doctors. People who try to seek health care often face language barriers at reception and in the consultation. Moreover, the effects of poverty, dependence on others, and lack of social support all affect these vulnerable people's health adversely.[5] Notwithstanding this, the primary care trust has managed to avoid compulsory patient assignments to Tower Hamlets practices in the past nine months.

Innovative methods of providing primary care to migrant populations and other groups who are difficult to reach, such as homeless people, already exist and continue to be developed within the NHS in east London, using personal medical services and alternative providers,[6] so the provision of yet another source of primary care by Médecins du Monde is not really the point.What, then, will this organisation offer? The detailed findings of the organisation's needs assessment exercise have not been made public, but seem to suggest that vulnerable people in east London need better advocacy rather than more clinical care. Questions remain about the organisation's arrangements for basic clinical investigations and access to secondary care. In addition, staffing these clinics might divert scarce doctors and nurses from mainstream care to more fragmented and rudimentary provision while general practices might refuse to register patients, assuming that the project will provide care instead.

Perhaps the main reason for the project is a tightening of the rules for eligibility to use the NHS. In

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